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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,819	06/07/2001	P. Scott White	S-94,664	1187

7590 05/18/2004
Ray G. Wilson
Los Alamos National Laboratory
LC/IP, MS A187
Los Alamos, NM 87545

EXAMINER

WILDER, CYNTHIA B

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/877,819

Applicant(s)

WHITE ET AL.

Examiner

Cynthia B. Wilder, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 6/11/2002.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's amendment to the specification filed on October 24, 2003 is acknowledged and has been entered. Claims 1-13 are pending and are discussed below.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-6, 9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ben-Dor et al. (Journal of Computational Biology, Vol. 7, Numbers 3/4, March 2000, pages 503-519) in view of Mitsuhashi et al (Nature, Vol. 367, pages 759-761, February 1994). Regarding claims 1-6, 9 and 13, Ben-Dor et al teach a method for identifying a set of sequences useful as address/capture tags (page 504) comprising the steps: (a) generating a chosen number of single-stranded, random oligonucleotide sequences having a chosen length (page 510, identification of substrings from the circular strings is generating subsequences of a given length), (b) rejecting

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all sequences which have a common subsequence to create a first remaining group of sequences (page 511-516, the entire method is designed to find non-overlapping probes by rejecting sequences which share "tokens", i.e., have identical sequences), (c) rejecting sequences which can form stable hairpin (page 518). Ben-Dor et al also teach rejection of sequences which form complementary sequences between tags (518). Ben-Dor et al expressly suggest synthesis of the oligonucleotides (page 518). Ben-Dor et al differs from the instant invention in that the reference does not expressly teach rejection of sequences which hybridize to non-target sequences, i.e., which form stable dimers with sequences that are not of interest nor melting temperature calculations.

In a general teaching of a new approach for designing oligonucleotide probes, Mitsuhashi et al teach rejection of probes which hybridize to non-target sequences including determination of the melting temperature of the different oligonucleotides and identifying oligonucleotides which have shared melting temperatures (page 759, columns 2 and 3). Mitsuhashi et al also teach a synthesis of the oligonucleotides (page 760). The reference further teach a selection of oligonucleotides with a melting temperature of 54 degrees Celsius to about 60 degrees Celsius (page 759, col. 3). Therefore, in view of the foregoing, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to utilize the method of Mitsuhashi et al. to reject undesirable address/capture tags generated by the method of Ben-Dor et al, since Ben-Dor sets out the problem ("Similar tags will necessarily entail cross-hybridization events (where tags hybridize to foreign anti-tags), reducing the accuracy and fidelity of the assay (page 506, lines 1-2)". Mitsuhashi et al solve this problem, stating "In addition to providing primer pairs that satisfy user-defined parameters such as length of primers,

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GC content, length of PCR products, the new design strategy described here provides homology information of all of the candidate primers, allowing users to know whether selected primer(s) will cross-hybridize to unrelated genes or not (page 759, column 2)". Thus Mitsuhashi solves the problem of Ben-Dor et al. by teaching how to identify oligonucleotides which form stable dimers and rejecting those which will cross-hybridize.

5. Claim 1-9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ben-Dor et al in view of Mitsuhashi et al as previously applied above and further in view of Southern et al. (US 5,770,367, June 23, 1998). Regarding claims 1-9 and 13, Ben-Dor et al in view of Mitsuhashi et al teach a method for identifying a set of sequences useful as address/capture tags comprising the limitations of claims 1-6, 9 and 13 previously discussed above. Ben-Dor et al in view of Mitsuhashi et al differ from the instant invention in that the references do not teach rejection of sequences which contains runs of nucleotides.

In a general teaching of tag reagents and assay methods of use, Southern et al teach sequences with runs of nucleotides which can cause problems in sequence analysis assays with arrays of oligonucleotides (col. 11, lines 23-30). It would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to have been motivated to have modified the method of Ben-Dor et al in view of Mitsuhashi et al to encompass a step of eliminating sequences runs in order to solve the problem identified by Southern of problems dealing with repeated sequences.

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6. Claims 1-6 and 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ben-Dor et al in view of Mitsuhashi et al as previously applied above and further in view of Nolan et al. (WO 99/22030, May 1999). Regarding claims 1-6 and 9-13, Ben-Dor et al in view of Mitsuhashi et al teach a method for identifying a set of sequences useful as address/capture tags comprising the limitations of claims 1-6, 9 and 13 previously discussed above. Ben-Dor et al in view of Mitsuhashi et al differ from the instant invention in that the references do not teach use of the oligonucleotides for flow cytometric detection of SNPs.

Nolan et al teach flow cytometric analysis of SNPs wherein tagged oligonucleotides are immobilized to plurality of identifiable microspheres (microparticles) (page 9 and example 4). It would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to have utilized the method of Ben-Dor et al in view of Mitsuhashi et al to select for primers for the flow cytometric analysis method of Nolan et al since Ben-Dor et al. notes "We derived and efficient construction for the design problem and prove that our construction is near-optimal (abstract)" while Mitsuhashi notes "In addition to providing primer pairs that satisfy user-defined parameters such as length of primers, GC content, length of PCR products, the new design strategy described here provides homology information of all the candidate primers, allowing users to know whether selected primer(s) will cross-hybridize to unrelated genes or not (page 759, col. 2)". Thus, an ordinary practitioner would have been motivated to use the design strategy of Ben-Dor et al in view of Mitsuhashi et al to achieve specific, efficient oligonucleotide selection for use un the method of Nolan et al.

Conclusion

7. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia B. Wilder
Patent Examiner
5/14/2009